

**NIH Office of Research on Women's Health  
U.S. Food and Drug Administration Office of Women's Health**

PRESENT

# 10<sup>TH</sup> ANNIVERSARY INTERDISCIPLINARY WOMEN'S HEALTH RESEARCH SYMPOSIUM



OCTOBER 24, 2013

MASUR AUDITORIUM

The Mark O. Hatfield Clinical Research Center  
National Institutes of Health • Bethesda, MD



**National Institutes of Health**  
*Office of Research on Women's Health*



**Office of  
Women's  
Health**



Specialized Centers of  
Research on Sex Differences



Building Interdisciplinary Research  
Careers in Women's Health

## DEAR RESEARCHERS, SCHOLARS, MENTORS, AND GUESTS:

It is with great pride that I welcome you to the 10th Anniversary Interdisciplinary Women's Health Research Symposium.

The NIH Office of Research on Women's Health (ORWH) initiated its research and career development programs based on a paradigm that views interdisciplinary approaches as essential to moving the science associated with women's health forward and to broadening the understanding of the contributions of sex and gender to human health and disease.

Today the scale and complexity of biomedical research demand that scientists move beyond the confines of their own disciplines. Interdisciplinary approaches integrate knowledge from multiple perspectives, resulting in more comprehensive and novel understanding of underlying biological processes.

ORWH recognizes that the study of women's health across the lifespan requires approaches that bridge and incorporate basic, clinical, and translational science. These approaches incorporate new models of collaboration, institutional support, and consider new ways of evaluating those who conduct such research.

"Team science" has advanced our understanding of sex and gender in disease processes, in biology, and in treatment responses. Today we recognize the truly innovative science and research emerging from the Specialized Centers of Research (SCOR) on Sex Differences, a unique initiative created by the Office of Research on Women's Health (ORWH). SCOR collaborations and creative approaches have expanded our knowledge base—and inform our next steps. The SCORs, now numbering 11 centers, are one of the many successes we celebrate at this symposium.

Today, we also celebrate the mentoring experience in another signature ORWH initiative: Building Interdisciplinary Research Careers in Women's Health program, known as "BIRCWH." The BIRCWH program connects early career stage researchers with senior investigators in a mentored relationship. It provides the framework for "BIRCWH scholars" to further develop their skills to become independent investigators while facilitating the infusion of interdisciplinary approaches to address relevant women's health research questions. Since its inception, the BIRCWH program has supported more than 542 early stage investigators through 77 awards at 39 academic institutions throughout the country. This unique interdisciplinary mentoring model has led to advances in sex and gender research in women's health. And, BIRCWH continues to advance our understanding of the importance of mentoring in all scientific fields.

I know you welcome as much as I do the opportunity to explore the innovative science presented today at the symposium and to recognize the investigators behind it who will lead us into the future—a future with science informed by sex and gender analysis at every stage.

Sincerely yours,



Janine A. Clayton, M.D.  
Director, Office of Research on Women's Health  
Associate Director for Research on Women's Health, NIH  
Department of Health and Human Services

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**WOMEN'S HEALTH RESEARCH**  
**SYMPOSIUM**

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## INTRODUCTION

ORWH continues to support innovative ways to encourage collaborative, interdisciplinary research that is team-based to improve women's health through two signature initiatives, the Specialized Centers of Research (SCOR) on Sex and Gender Factors Affecting Women's Health and the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program.

## SPECIALIZED CENTERS OF RESEARCH ON SEX DIFFERENCES

The Specialized Centers of Research on Sex Differences represent an innovative interdisciplinary research program focusing on sex differences and major medical conditions affecting women. The SCOR program supports accomplished scientists who conduct research that integrates basic, clinical, and translational research at P50 centers. ORWH developed and implemented the SCOR program in 2002 to increase the transfer of basic research findings into clinical practice, which considers male/female differences. ORWH serves as the program's coordinator, overseeing the progress in advancing sex differences research across the centers, while the day-to-day programmatic management of the SCORs resides in the participating ICs.

## BUILDING INTERDISCIPLINARY RESEARCH CAREERS IN WOMEN'S HEALTH

ORWH designed, developed, and implemented the BIRCWH K12 Program in 1999 to increase the number of women's health researchers working in a mentored interdisciplinary environment. BIRCWH supports junior faculty members who have recently completed clinical training or postdoctoral fellowships and who are beginning basic, translational, clinical, and/or health services research related to women's health research by pairing junior researchers with senior investigators. BIRCWH is built on three pillars: strong mentoring, interdisciplinary research, and career development. Programs accomplish these goals by ensuring that mentors represent diverse disciplines needed to carry out interdisciplinary projects that will bridge training with research independence for BIRCWH scholars.

The program continues to expand the network of scientists and clinicians who have the interdisciplinary research skills needed to further the study of women's health and sex differences. Currently, there are 29 active BIRCWH programs across the country. The majority of scholars have gone on to receive funding from NIH, research foundations, or the industry.

ORWH is responsible for the programmatic aspects of the BIRCWH program, and the grants management aspects reside within the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Institute on Drug Abuse (NIDA), and the National Institute of Environmental Health Sciences (NIEHS). The first BIRCWH grants were awarded in FY 2000.



## WOMEN'S HEALTH AND SEX DIFFERENCES RESEARCH: PAST, PRESENT & FUTURE

The 10th Anniversary Interdisciplinary Women's Health Research Symposium is an opportunity not only to recognize and share current research efforts, but also to reflect on how past efforts have informed the directions future research will take.

The NIH strategic plan for women's health research, *Moving Into the Future with New Dimensions and Strategies for Women's Health Research: A Vision for 2020 for Women's Health Research*, calls for an increased focus on sex and gender differences in basic science research to better understand their significance in health and disease.

Research conducted with both female and male cells tissues and animal model systems, is paramount for developing strategies to inform sex- and gender-appropriate medicine, including clinical diagnosis and therapy. The study of biological, behavioral, and social variables and how they interact with environmental, age, sex, and other factors is integral to the development of an expanded multidimensional scientific knowledge base.

### NIH STRATEGIC GOALS FOR WOMEN'S HEALTH AND SEX DIFFERENCES RESEARCH

1. Increase sex differences research in basic science studies.
2. Incorporate findings of sex/gender differences in the design and application of new technologies, medical devices, and therapeutics to inform and improve women's health.
3. Actualize personalized prevention, diagnostics, and therapeutics for girls and women.
4. Create strategic alliances and partnerships to maximize the domestic and global impact of women's health research.
5. Develop and implement new communication and social networking technologies to increase understanding and appreciation of women's health and wellness research.
6. Employ innovative strategies to build a well-trained, diverse, and vigorous women's health research workforce.

Cosponsors with ORWH for SCOR and BIRCWH include the National Cancer Institute (NCI), National Institute on Aging (NIA), the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Environmental and Health Sciences (NIEHS), the Office of Dietary Supplements (ODS), and the U.S. Food and Drug Administration (FDA).

## Agenda

### OFFICE OF RESEARCH ON WOMEN'S HEALTH

## TENTH ANNIVERSARY INTERDISCIPLINARY WOMEN'S HEALTH RESEARCH SYMPOSIUM

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### Agenda

#### Thursday, October 24, 2013

The Mark O. Hatfield Clinical Research Center  
Masur Auditorium  
Bethesda, MD

8:00–8:30 a.m.	<b>Registration</b>
8:30–9:00 a.m.	<b>Welcome and Opening Remarks</b> <b>Janine A. Clayton, M.D.</b> , Associate Director for Research on Women's Health; Director of the Office of Research on Women's Health (ORWH), National Institutes of Health (NIH)  <b>Pamela E. Scott, Ph.D.</b> , Director for Research and Development on Women's Health, Office of Women's Health (OWH), Food and Drug Administration (FDA)
9:00–9:40 a.m.	<b>Podium Presentations—Session I: Stress, Hormones, Cognition, and Women's Health</b> <i>10-minute presentations with 5 minutes for Q&amp;A</i>  <b>Moderator: Kathleen M. O'Leary, M.S.W.</b> , National Institute of Mental Health (NIMH)
9:00–9:10 a.m.	<i>Early Adverse Life Events: Influence on Resting State Connectivity in Patients with Chronic Abdominal Pain</i> <b>Arpana Gupta, M.D.</b> , Specialized Center of Research (SCOR), University of California, Los Angeles
9:15–9:25 a.m.	<i>Early Life Adversity Increases Risk of New-Onset Depression During the Menopause Transition</i> <b>C. Neill Epperson, M.D.</b> , SCOR, Perelman School of Medicine, University of Pennsylvania
9:30–9:40 a.m.	<i>The Impact of Worry on Error-Related Brain Activity and Behavioral Performance Is Moderated by Hormonal Contraceptive Use</i> <b>Jason Moser, Ph.D.</b> , Building Interdisciplinary Research Careers in Women's Health (BIRCWH), Department of Psychology, Michigan University
9:45–10:00 a.m.	<b>BREAK</b>



## Agenda

- 10:00–10:45 a.m.**      **Podium Presentations—Session II: The Intersection of Reproductive Health Aspects and Women’s Health**  
*10-minute presentations with 5 minutes for Q&A*
- Moderator: Estella Parrott, M.D., M.P.H., Eunice Kennedy Shriver**  
National Institute of Child Health and Human Development (NICHD)
- 10:00–10:10 a.m.      *Drug Treatment for Type 2 Diabetes Modifies Fibroid Risk*  
**Digna R. Velez Edwards, Ph.D.,** BIRCWH, Vanderbilt Epidemiology Center, Institute for Medicine and Public Health Center
- 10:15–10:25 a.m.      *Why Normal Pregnancy Is Protective Against Maternal Hypertension Later in Life*  
**Egle Bytautiene, M.D., Ph.D.,** BIRCWH, University of Texas Medical Branch at Galveston
- 10:30–10:40 a.m.      *Exposure to Prenatal Life Events Stress Is Associated with Masculinized Play Behavior in Girls*  
**Emily Barrett, Ph.D.,** BIRCWH, University of Rochester
- 10:45 a.m.–11:45 a.m.**      ***Special Panel—The Art and Science of Interdisciplinary Research***
- Scott Hultgren, Ph.D.,** Washington University in St. Louis  
**Carolyn Mazure, Ph.D.,** Yale School of Medicine  
**Julienne Rutherford, Ph.D.,** University of Illinois at Chicago
- 11:45 a.m.–1:00 p.m.**      **LUNCH; View BIRCWH and SCOR Program Posters**
- 1:00–1:45 p.m.**      **Keynote Presentation**
- Introduction*  
**Janine A. Clayton, M.D.,** ORWH
- The Art and Science of Interdisciplinary Research—Lessons Learned from NCCAM’s First Decade***  
**Josephine P. Briggs, M.D.,** Director, National Center for Complementary and Alternative Medicine (NCCAM)
- 1:45–2:00 p.m.**      **BREAK**
- 2:00–2:45 p.m.**      **Podium Presentations—Session III: Addictive Disorders and Women’s Health**  
*10-minute presentations with 5 minutes for Q&A*
- Moderator: Cora Lee Wetherington, Ph.D.,** National Institute on Drug Abuse (NIDA)



## Agenda

- 2:00–2:10 p.m. *Targeting the Noradrenergic System for Gender-Sensitive Treatment Development for Tobacco Dependence*  
**Sherry A. McKee, Ph.D. Clin.**, SCOR, Yale University School of Medicine
- 2:15–2:25 p.m. *Varenicline Versus Nicotine Patch for Smoking Cessation in Women: Efficacy Findings for a 4-Week Double-Blind Trial*  
**Erin McClure, Ph.D.**, SCOR, Medical University of South Carolina
- 2:30–2:40 p.m. *Sex Differences in Anticipatory Negative Contrast and Binge-Like Eating Behaviors in Mice*  
**Tomoko Udo, Ph.D., M.Sc.**, BIRCWH, Department of Psychiatry, Yale University of School of Medicine
- 2:45–3:30 p.m. Podium Presentations—Session IV: Women’s Health in the Middle Years**  
*10-minute presentations with 5 minutes for Q&A*
- Moderator: Joan D. Nagel, M.D., M.P.H.**, ORWH
- 2:45–2:55 p.m. *The Role of Loading Mechanics in Sex Differences of Knee Osteoarthritis*  
**Melissa Morrow, Ph.D.**, BIRCWH, Mayo Clinic
- 3:00–3:10 p.m. *Association of Urinary Phthalate Levels with Metabolic Syndrome Among Women and Men in NHANES 1999–2008*  
**Aditi Saxena, M.D.**, BIRCWH, Division of Endocrinology, Harvard Medical School
- 3:15–3:25 p.m. *The Dek Oncogene Drives Breast Cancer Progression and Chemotherapeutic Resistance*  
**Lisa M. Privette Vinnedge, Ph.D.**, BIRCWH, Cincinnati Children’s Hospital Medical Center
- 3:30 p.m. Closing Remarks and Adjournment**  
**Joan D. Nagel, M.D., M.P.H.**, ORWH





## PRESENTER ABSTRACTS

### Exposure to Prenatal Life Events Stress Is Associated with Masculinized Play Behavior in Girls

Emily S. Barrett (presenting author),<sup>1</sup> Fan Liu,<sup>2</sup> Christina Wang,<sup>3</sup> and Shanna H. Swan<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, University of Rochester School of Medicine and Dentistry; <sup>2</sup>Department of Preventive Medicine, Icahn School of Medicine at Mount Sinai; and <sup>3</sup>Division of Endocrinology, Department of Medicine, Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute

**Background and Objective:** Previous research on humans and animal models suggests that exposure to prenatal stress not only affects fetal development, but also can do so in different ways in males and females. Only one published study has prospectively examined the relationship between exposure to prenatal stress and gender-specific play behavior during childhood, finding masculinized play behavior in girls who experienced high prenatal life events stress, but no associations in boys. Here we examine the relationship between exposure to prenatal stress and play behavior during childhood in a second prospective cohort from the Study for Future Families.

**Methods:** Pregnant women completed questionnaires on stressful life events during pregnancy, and those who reported 1 or more stressors were considered highly stressed. Families were re-contacted several years later (mean age of index child: 4.9 years), and mothers completed a questionnaire including the validated Preschool Activities Inventory (PSAI), which measures sexually dimorphic play behavior.

**Results:** In sex-stratified analyses, after adjusting for child's age, parental attitudes toward gender-atypical play, age and sex of siblings, and other relevant covariates, girls ( $n = 72$ ) exposed to high prenatal life events stress had higher scores on the PSAI masculine sub-scale ( $\beta = 3.48$ ,  $P = .006$ ) and showed a trend towards higher (more masculine) composite scores ( $\beta = 2.63$ ,  $P = .08$ ). By contrast, in males ( $n = 74$ ), prenatal stress showed a trend towards association with higher PSAI feminine sub-scale scores ( $\beta = 2.23$ ,  $P = .10$ ), but no association with masculine or composite scores.

**Conclusions:** These data provide further evidence that prenatal stress may have androgenic effects on

female fetuses and anti-androgenic effects on male fetuses.

### Why Normal Pregnancy Is Protective Against Maternal Hypertension Later in Life

Egle Bytautiene (presenting author), Michael Wen, Talar Kechichian, Phyllis Gamble, Esther Tamayo, and George R. Saade

Department of Obstetrics and Gynecology, University of Texas Medical Branch

**Background and Objective:** We have previously shown that a normal pregnancy is protective against hypertension later in life in both obese and non-obese animals. The objective was to investigate if alterations in the renin-angiotensin system could explain the protective effect of pregnancy.

**Methods:** Virgin CD-1 female mice were placed on standard fat (SF) or high fat (HF) diets. After 3 months, mice were randomly allocated to a breeding versus non-breeding group, resulting in 4 groups: primigravid on SF (SF-PG) or HF (HF-PG) and nulligravid on SF (SF-NG) or HF (HF-NG). The primigravid group proceeded through a normal pregnancy and delivery. After weaning, all animals were contemporaneously placed on a SF diet. Visceral adipose tissue (VAT) and kidneys were collected from PG at 6 months post partum and from age-matched NG mice. Protein expressions of angiotensin (ANG) and its receptors, angiotensin receptor 1 and 2 (AT1 and AT2, respectively), were determined using Western blot analysis. One-way ANOVA and Kruskal Wallis tests with appropriate posthoc tests were used for statistical analysis (significance  $P < 0.05$ ).

**Results:** There were no differences in ANG protein expression between groups, neither in VAT nor kidneys. AT1 was significantly higher in VAT from SF-NG groups than from SF-PG. In kidneys, AT1 was significantly higher in both NP groups compared to the PG groups. AT2 was significantly lower in both NG groups in VAT and kidney compared with PG.

**Conclusions:** The protective effect of a normal pregnancy could be mediated by a decrease in AT1 receptors and an increase in AT2 receptors in the kidney and VAT.



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## Drug Treatment for Type 2 Diabetes Modifies Fibroid Risk

Digna R. Velez Edwards (presenting author),<sup>1</sup>  
Katherine E. Hartmann,<sup>2</sup> Anushi Shah,<sup>3</sup> Hua  
Xu,<sup>4</sup> and Todd L. Edwards<sup>1</sup>

<sup>1</sup>Center for Human Genetics and <sup>2</sup>Department  
of Obstetrics and Gynecology, Institute for  
Medicine and Public Health, Vanderbilt  
Epidemiology Center, <sup>3</sup>Department of  
Biomedical Informatics, Vanderbilt University,  
<sup>4</sup>School of Biomedical Informatics, University of  
Texas Health Science Center, Houston

**Background and Objective:** Uterine fibroids (UFs) affect 77% of women by menopause, and account for \$9.4 billion in yearly health care costs. Studies have shown that type 2 diabetes (T2D) associates with UF protection. Whether protection derives from having T2D or T2D pharmacologic management (treatment) is unclear. The objective was to further evaluate the relationship between UFs and T2D treatment.

**Methods:** UF status was determined from pelvic imaging. Women with T2D were identified from their clinical records and had not been diagnosed with UFs at T2D diagnosis. Cox regression, adjusted for confounders, was used to test for association between UF presence and T2D treatments (metformin [n = 1,089], thiazolidinedione [n = 353], insulin [n = 1,477], or other treatment [n = 332]). We also tested for interactions between T2D treatment and race and body mass index.

**Results:** We identified 2,321 women with T2D, with average age of diagnosis of 47. Seventeen percent developed UFs after T2D diagnosis. Insulin, compared to other treatments, conferred protection from UFs in European Americans (EAs) and African Americans (AAs) (EAs, adjusted hazard ratio [aHR] = 0.50, 95% confidence interval [CI] 0.36-0.69; AA, aHR = 0.53, 95% CI 0.37-0.74). We observed increased UF risk with metformin treatment among EAs (aHR = 1.94, 95% CI 1.37-2.74), but not among AAs (aHR = 1.07, 95% CI 0.76-1.51). Normal weight and overweight T2Ds had the most protection from UFs due to insulin compared to obese T2Ds. Thiazolidinedione and other T2D treatments did not associate with UFs.

**Conclusions:** These data support the hypothesis that protection from UFs linked to T2D diagnosis may derive from T2D treatments, specifically insulin. Further research is required to dissect the biological mechanisms of this effect, as well as the link between metformin and UF risk.

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## Early Life Adversity Increases Risk of New Onset Depression During the Menopause Transition

C. Neill Epperson (presenting author)

Perelman School of Medicine, University of  
Pennsylvania

**Background and Objective:** There is an increased risk for new onset depression during the menopause transition, even in women without previous psychiatric history. Childhood adversity has lasting effects on neurotransmitter systems, which are also modulated by estrogen. We sought to determine whether early life adversity contributes to the increased risk of incident menopause depression.

**Methods:** In a 15-year longitudinal study of women undergoing a natural transition to menopause, participants (n = 390) completed the Clinical Epidemiologic Scale for Depression (CES-D). A CES-D score higher than 16 was used to denote a probable major depressive episode. The Adverse Childhood Events (ACE) questionnaire was used to assess the presence of abuse, neglect, and serious family dysfunction experienced prior to the age of 18. Of the 390 participants with at least 2 mood assessments, 206 of the women who remain in the study have been contacted to collect ACE information. The impact of number of ACEs (0, 1, 2, or more) on new onset depression across the five stages of menopause (premenopause, late premenopause, early transition, late transition, postmenopause) was determined.

**Results:** There were 1,033 observations with each individual contributing on average 12 observations. Using generalized estimating equations and controlling for age, menopause stage was associated with a 2.7-fold risk ( $P = .02$ ) of new onset depression as women progressed from the pre- to postmenopause.

**Conclusions:** Childhood adversity, defined broadly, is a risk factor for first episode depression during the menopause transition when ovarian sources of estrogen are waning. These data suggest an

environment by hormone interaction predicting depression risk in menopausal women.

## Varenicline Versus Nicotine Patch for Smoking Cessation in Women: Efficacy Findings from a 4-Week Double-Blind Trial

Kevin M. Gray (presented by Erin McClure, Ph.D.)<sup>1</sup>, Michael E. Saladin,<sup>1</sup> Nathaniel L. Baker,<sup>1</sup> Erin A. McClure,<sup>1</sup> Karen J. Hartwell,<sup>1,2</sup> and Matthew J. Carpenter<sup>1</sup>

<sup>1</sup>Medical University of South Carolina; and

<sup>2</sup>Ralph H. Johnson Veterans Affairs Medical Center

**Background and Objective:** Women may have more difficulty quitting smoking than men; comparative evaluation of cessation pharmacotherapies in women may be critical to inform clinical practice. Within a parent study examining ovarian hormone effects on smoking cessation, we conducted the first double-blind trial directly comparing the efficacy of varenicline versus nicotine patch.

**Methods:** Treatment-seeking nicotine-dependent female smokers (aged 18-45, n = 137) were randomized to receive a 4-week course of (a) varenicline tablets and placebo patches or (b) placebo tablets and nicotine patches, via a double-blind, double-dummy design. All participants received a 1-week titration lead-in (tablets only) before a targeted quit date, followed by goal dosing (tablets and patches) for an additional 4 weeks. All participants received 2 brief cessation counseling sessions. Abstinence was assessed at weekly visits and analyzed via an intent-to-treat approach.

**Results:** During the last week of the 4-week treatment, 46.9% of varenicline participants achieved 7-day point prevalence abstinence, compared with 20.6% of nicotine patch participants (OR 3.3 [95% CI 1.5-6.9];  $P = .002$ ). At the end of a 4-week post-treatment follow-up, 7-day point prevalence abstinence numerically favored varenicline, but did not meet statistical significance (23.4% vs. 13.7%, OR 1.9 [95% CI 0.8-4.7];  $P = 0.15$ ).

**Conclusions:** Varenicline, compared with nicotine patch, more than doubled the odds of abstinence at end of 4-week treatment. Absolute abstinence rates with both treatments were lower than those in a prior open-label trial inclusive of both men and women (Aubin et al., 2008). Nonetheless, these preliminary

findings support varenicline as a preferred pharmacotherapy for smoking cessation in women.

*Funding sources: NIDA P50DA16511 Component 4 (KMG & MES), NIDA K23DA020482 (MJC), and NCRR UL1RR029882 (MUSC Clinical and Translational Research Center). Varenicline and matched placebo were supplied by Pfizer, Inc.*

## Early Adverse Life Events: Influence on Resting State Connectivity in Patients with Chronic Abdominal Pain

Arpana Gupta (presenting author)

University of California, Los Angeles

**Background and Objective:** Early adverse life (EAL) events and female sex have been identified as a vulnerability factor for the development of several stress-sensitive disorders, including irritable bowel syndrome (IBS). Methylation of genes related to the central stress system have been implicated as an epigenetic mechanism mediating this association. We aimed to identify disease and sex-based differences in resting state (RS) connectivity associated with EALs in IBS subjects.

**Methods:** Resting state functional magnetic resonance imaging was used to identify patterns of intrinsic brain oscillations in the form of RS networks in 168 subjects (58 IBS, 28 female; and 110 healthy controls, 72 female). Partial Least Squares (PLS) multivariate analysis was used to identify possible correlations between functional connectivity in 7 identified RS network components (pain, emotion, salience/executive control, cognition, cognition and language, cognitive control, and the default mode network) and a history of EAL. Disease and sex-related effects of EAL on RS networks were observed.

**Results:** While a history of EALs was associated with altered connectivity in the salience/executive control network to a similar extent in male and female IBS patients, male IBS patients demonstrated additional EAL-related alterations in the cerebellar network. This study is the first to identify correlations between RS networks and EALs in IBS subjects.

**Conclusions:** These results suggest that exposure to EALs before age 18 can shape adult RS in both male and female patients in the salience network, a brain



network that has been implicated in the pathophysiology of central pain amplification.

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## Targeting the Noradrenergic System for Gender-Sensitive Treatment Development for Tobacco Dependence

Sherry A. McKee (presenting author)  
Yale University School of Medicine

**Background and Objective:** Tobacco use is the leading cause of preventable morbidity and mortality in the United States. Women, compared to men, have poorer rates of smoking cessation, exacerbated health risks, and appear to have less success with available first-line treatments. However, few attempts have been made to develop gender-sensitive smoking cessation treatments. The considerable body of data suggesting that women are more likely to smoke to regulate negative affect and stress, while men are more likely to smoke for the reinforcing properties of nicotine, suggests an important direction in the development of a new approach to smoking cessation treatments. Substantial preclinical evidence demonstrates that noradrenergic transmission is involved in stress-induced relapse and nicotine-related reinforcement, yet there is a surprising lack of clinical investigations translating these findings to humans.

**Methods:** Using a hybrid human laboratory and clinical outcome design, we have evaluated effects of noradrenergic targets including guanfacine (alpha2a agonist), prazosin (alpha1 antagonist), and carvedilol (combined alpha1 and beta antagonist) on stress-reactivity, smoking-related reinforcement, and reductions in cigarette use.

**Results:** There were notable differences in results across the noradrenergic targets with guanfacine producing the most promising findings to date. Guanfacine significantly reduced smoking behavior during the treatment phase in both women and men, but preferentially improved laboratory-based assessments of stress-reactivity in women and smoking-related reinforcement in men.

**Conclusions:** Noradrenergic agonists, especially alpha2a noradrenergic agonists, are a highly promising neurobiological target for the development of gender-sensitive therapeutics for smoking cessation.

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## The Role of Loading Mechanics in Sex Differences of Knee Osteoarthritis

Melissa M. B. Morrow (presenting author),<sup>1</sup>  
Mary I. O'Connor,<sup>2</sup> and Kenton R. Kaufman<sup>1</sup>

<sup>1</sup>Department of Orthopedic Surgery, Mayo Clinic (Rochester, MN); and <sup>2</sup>Department of Orthopedic Surgery, Mayo Clinic (Jacksonville, FL)

**Background and Objective:** Women have a higher incidence of knee osteoarthritis (KOA) than men do. Mechanisms attributing to this difference are unclear. We hypothesize that the difference could result in part from loading mechanics placed on the knee during walking. The objective was to characterize and compare knee loading mechanics between adult men and women with medial KOA.

**Methods:** Adults (221 women and 73 men) with medial compartment KOA underwent bilateral knee x-rays to determine radiographic OA severity and cartilage thickness. Gait analysis was performed during level walking to determine measures of cadence, magnitude of knee loading, rate of knee loading, and timing of peak loads during the gait cycle. ANCOVA analyses were performed to test the main effects of sex on gait. Results were adjusted for OA severity, age, body mass index, and knee alignment.

**Results:** Medial compartment cartilage thickness and estimated loading during walking were lower in women compared to men. There was no sex difference in the ratio of medial compartment cartilage thickness to medial compartment loading or in loading rates. Women walked with a faster cadence, and women applied peak loads during terminal stance, while men tended to apply peak loads during the initial loading response after heel strike.

**Conclusions:** Knee loading rate and magnitude are not indicated as risk factors in women; however, over a constant distance, women take more steps than men and experience peak loading later in the gait cycle. Differences in cumulative loading mechanics could contribute to sex differences in the onset and progression of KOA.

## The Impact of Worry on Error-Related Brain Activity and Behavioral Performance Is Moderated by Hormonal Contraceptive Use

Jason Moser (presenting author), Hans Schroder, and Tim Moran

Michigan State University

**Background and Objective:** Chronic worriers, “individuals characterized by repetitive, uncontrollable anxious thoughts,” show enhanced brain activity to errors, suggesting they invest greater neural resources to bounce back from mistakes. Recently, we showed that the relationship between worry and enhanced error-related brain activity is several times greater in women than men, consistent with other behavioral research indicating that worry may have a disproportionately negative impact on women. Together, these findings suggest that female-specific factors may contribute to the impact of worry on error-related brain activity and behavioral performance. The objective of the study was to test the hypothesis that endogenous ovarian hormone fluctuations contribute to the impact of worry on error-related brain activity and performance.

**Methods:** Twenty-seven undergraduate women not taking hormonal contraceptives and 13 undergraduate women taking hormonal contraceptives performed a standard reaction time task while error-related brain activity was recorded. Following the task, they completed the Penn State Worry Questionnaire to measure worry levels.

**Results:** Women not taking hormonal contraceptives showed the expected associations such that higher worry scores were related to enhanced error-related brain activity ( $r = .45$ ) and poorer behavioral performance ( $r = -.55$ ). Importantly, women taking hormonal contraceptives did not demonstrate significant associations between worry and error-related brain activity ( $r = .22$ ) or worry and behavioral performance ( $r = .29$ ).

**Conclusions:** Findings from the current study suggest that the effect of worry on error-related brain activity and performance may depend on naturally fluctuating ovarian hormones. Hormone therapy may be one viable option for reducing the negative impact of worry on cognitive functioning.

## Association of Urinary Phthalate Levels with Metabolic Syndrome Among Women and Men in NHANES 1999–2008

Aditi Saxena (presenting author), Tamarra Jamestodd, and Ellen Seely

Harvard Medical School

**Background and Objective:** Increased exposure to certain phthalates is associated with increased risk of diabetes and insulin resistance; however, association with metabolic syndrome, a harbinger of future cardiovascular disease, has not been examined. The purpose of the study was to conduct an exploratory analysis evaluating associations between urinary phthalate metabolites with the presence of metabolic syndrome and its components, with focus on sex differences.

**Methods:** We analyzed men and women aged 20 to 80 years, in NHANES 1999-2008 ( $n = 2611$ ). Logistic regression assessed the relationship individually between 8 urinary phthalate metabolites and presence of metabolic syndrome (yes/no), controlling for urinary creatinine and age. Stratified analyses provided sex-specific estimates of association.

**Results:** Both MEP and MiBP were associated with increased risk of metabolic syndrome, whereas MBzP, MnBP, MCPP and  $\Sigma$ DEHP were not. In the overall population, both MEP and MiBP conferred increased risk of metabolic syndrome, OR 1.44 (1.10, 1.89),  $P = .008$  for MEP, and OR 1.27 (1.004, 1.61),  $P = .045$  for MiBP, though odds varied by sex and levels of exposure. Men in the highest quartile of exposure to MEP had significantly greater odds of metabolic syndrome (OR 1.52, [1.07, 2.18],  $P = .02$ ). In women, MEP exposure was not associated with metabolic syndrome. Conversely, MiBP exposure was associated with increased risk of metabolic syndrome in women, OR 1.58, (1.10, 2.27),  $P = .01$ , but not in men.

**Conclusions:** Urinary phthalate metabolites are associated with metabolic syndrome, but the strength of association varies by specific phthalate exposure and sex. Metabolic syndrome portends future cardiovascular risk. Mechanisms linking phthalate exposure to cardiovascular disease require further investigation.



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## Sex Differences in Anticipatory Negative Contrast and Binge-Like Eating Behaviors in Mice

Tomoko Udo (presenting author), Darren M. Opland, and Ralph J. DiLeone

*Department of Psychiatry, Yale University of School of Medicine*

**Background and Objective:** Women may be more susceptible to maladaptive eating behaviors, such as binge eating disorder, than men. However, due to primary focus on female sample, there are few preclinical and clinical studies on sex differences in binge-like eating behaviors. The study aimed to examine sex differences in adaptation of feeding behaviors under limited access to palatable food in mice, using Anticipatory Negative Contrast (ANC). In addition to binge-like eating, ANC models behavioral inhibition, and thus allows modeling regulation of food intake in general as well.

**Methods:** In ANC, male and female C57BL/6J mice are given access to food for two consecutive 5-minute periods. They received either regular chow only (chow/chow [CC]; n = 5 per sex) or chow followed by palatable chocolate pellets (chow/sucrose [CS]; n = 5 per sex). Following several pairings, CS mice learn to decrease chow intake in anticipation of palatable food and consequently binge-eat the palatable food, compared with CC mice.

**Results:** For all mice, daily calorie intake was restricted to maintain 80% to 85% free-feeding body weight. The first feeder and second feeder intakes were compared by feeding condition and by sex. In anticipation of access to palatable foods, both male and female CS mice showed significantly less intake of regular chow, compared with their CC counterparts. Across sex, the CS group also developed binge-like eating of preferred food. Although there was no significant difference in the level of suppression of the first feeder intake (i.e., regular chow) by sex, female CS mice consumed significantly more preferred food than male CS mice during the second 5-minute feeding period. Thus, while no sex differences were found in the ability to inhibit food intake, female mice appeared to have developed more escalated binge-like eating behaviors than male mice.

**Conclusions:** This is the first study to demonstrate greater vulnerability to binge-like eating in females

than in males using the ANC paradigm. This project will be followed by characterizing the neural circuitry underlying sex differences in behavioral adaptations observed in ANC. Identifying neurobiological systems involved in self-regulation of food intake and binge eating behaviors may ultimately lead to new sex-specific therapeutic targets for intervention against binge eating and eating disorders in general.

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## The Dek Oncogene Drives Breast Cancer Progression and Chemotherapeutic Resistance

Lisa M. Privette Vinnedge (presenting author),<sup>1</sup> Purnima K. Wagh,<sup>1</sup> Juana Serrano-Lopez,<sup>1</sup> Susan E. Waltz,<sup>1</sup> and Susanne I. Wells<sup>2</sup>

<sup>1</sup>Cincinnati Children's Hospital Medical Center, and <sup>2</sup>University of Cincinnati

**Background and Objective:** Late-stage breast cancer (BC) patients are faced with poor survival rates, drug resistance, and risk of tumor recurrence. Novel drivers of advanced disease must be identified that also may be targets of new therapies. This study was needed to investigate an oncogene that may determine disease progression and drug resistance. The goal was to determine if the Dek oncogene was required for breast cancer progression in vivo and drug resistance. Furthermore, we studied the role of Dek in maintaining the breast cancer stem cell population, which has been implicated as the causative factor for drug resistance and disease recurrence.

**Methods:** Dek<sup>-/-</sup> mice were bred to the MMTV-Ron breast cancer model. Histological and biochemical analyses were performed on tissues and cell lines derived from murine tumors.

**Results:** Dek expression is upregulated upon Ron receptor activation. Loss of the Dek oncogene significantly delayed tumor initiation in vivo due, in part, to decreased proliferation in pre-neoplastic glands. In cell lines derived from the murine model, Dek loss was associated with decreased BCSC numbers, fewer overt lung metastases, and Wnt pathway inhibition. Finally, the loss of Dek enhanced the cytotoxicity of cisplatin.

**Conclusions:** Dek is an important driver of BC progression and supports the maintenance of the BCSC population, which is thought to be responsible for disease recurrence and drug resistance. Targeted genetic inhibition of Dek may enhance therapeutic



response to several classes of drugs. Pre-clinical testing of DEK inhibition should proceed as a method to enhance drug sensitivity in BCSCs, thus resulting in improved survival.





## PRESENTER BIOGRAPHIES

### Emily Barrett, Ph.D.

Emily Barrett, Ph.D., is an assistant professor of obstetrics and gynecology and a member of the Environmental Health Sciences Center faculty at the University of Rochester School of Medicine and Dentistry. Dr. Barrett received her Ph.D. in biological anthropology from Harvard University, where she studied how ecological factors affect the female reproductive system. Her current research builds on that by looking at how exposure to stress and endocrine disruptors (particularly phthalates) affects the health of pregnant women and their children. Dr. Barrett is particularly interested in reproductive health and sexually dimorphic outcomes. She is the director of the Rochester, NY, center of The Infant Development and the Environment Study (TIDES).

### Josephine Briggs, M.D.

Josephine Briggs, M.D., an accomplished researcher and physician, received her A.B. in biology from Harvard-Radcliffe College and her M.D. from Harvard Medical School. She completed her residency training in internal medicine and nephrology at the Mount Sinai School of Medicine, followed by a fellowship at Yale, and she then worked as a research scientist at the Physiology Institute at the University of Munich.

In 1985, Dr. Briggs moved to the University of Michigan, where she held several academic positions, including associate chair for research in the Department of Internal Medicine and professorships in the Division of Nephrology, Department of Internal Medicine, and the Department of Physiology. She joined the National Institutes of Health (NIH) in 1997 as director of the Division of Kidney, Urologic, and Hematologic Diseases at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In 2006, Dr. Briggs accepted a position as senior scientific officer at the Howard Hughes Medical Institute. In January 2008, she returned to NIH as the Director of the National Center for Complementary and Alternative Medicine.

Dr. Briggs has published more than 175 research articles, book chapters, and scholarly publications and has served on the editorial boards of several journals; she was deputy editor for the *Journal of Clinical Investigation*. Dr. Briggs is an elected member of the American Association of Physicians and the American Society of Clinical Investigation and a fellow of the American Association for the Advancement of Science. She has received many

awards and prizes, including the Volhard Prize of the German Nephrological Society, the Alexander von Humboldt Scientific Exchange Award, and NIH Director's Awards for her role in the development of the Trans-NIH Type I Diabetes Strategic Plan and her leadership of the Trans-NIH Zebrafish committee. Dr. Briggs is also a member of the NIH Steering Committee, NIH's senior governing board.

### Egle Bytautiene, M.D., Ph.D.

Egle Bytautiene, M.D., Ph.D., received her M.D. from the Medical Faculty of Vilnius University in Lithuania in 1991. In 1997, she joined the Department of Obstetrics and Gynecology at the University of Texas Medical Branch (UTMB). Over the next 15 years, she rose from research fellow to assistant professor in the same department. In addition, in 2010, she graduated from the Graduate School of Biomedical Sciences at UTMB and was awarded a Ph.D. in clinical sciences. Dr. Bytautiene has dedicated her research career to women's health. Her interests range from preterm birth—in 2000 she published on a novel animal model for allergy-induced preterm birth—to preeclampsia, for which she received an NIH R03 grant to study long-term maternal health in a mouse model of preeclampsia with preexisting prepregnancy obesity. Her Ph.D. dissertation focused on long-term outcomes in offspring exposed to preeclampsia and prepregnancy obesity. There is no known mechanism to prevent preeclampsia, but obesity could be managed by lifestyle modification or medications, so after completing her Ph.D., Dr. Bytautiene decided to focus on metabolic syndrome research with special interest in prepregnancy obesity. Under guidance of her long-time mentor, Dr. George Saade, Dr. Bytautiene has developed and continue to work on a mouse model to study long-term maternal consequences of prepregnancy obesity. In October 2011, she was appointed as a BIRCWH Scholar. BIRCWH support has allowed her to concentrate on analyzing data that she has accumulated and on developing grant applications. She credits UTMB's BIRCWH, and especially its director, Dr. Abby Berenson, for her achievements and success.

### Janine A. Clayton, M.D.

Janine A. Clayton, M.D., a board-certified ophthalmologist, is the author of more than 80 scientific publications, journal articles, and book chapters. Prior to joining the Office of Research on Women's Health, she was the Deputy Clinical



Director of the National Eye Institute (NEI) at NIH. Dr. Clayton's research interests include autoimmune ocular diseases and the role of sex and gender in health and disease. Dr. Clayton has a particular interest in ocular surface disease, and she discovered a novel form of disease associated with premature ovarian insufficiency that affects young women.

A native Washingtonian, Dr. Clayton received her undergraduate degree with honors from the Johns Hopkins University, and her medical degree from Howard University College of Medicine. She completed a residency in ophthalmology at the Medical College of Virginia and fellowship training in Cornea and External Disease at the Wilmer Eye Institute at Johns Hopkins Hospital, and in Uveitis and Ocular Immunology at NEI. Dr. Clayton has been an attending physician and clinical investigator in cornea and uveitis at the NEI since 1996, conducting research on inflammatory diseases of the anterior segment. Her clinical research has ranged from randomized controlled trials of novel therapies for immune mediated ocular diseases to studies on the development of digital imaging techniques for the anterior segment.

Dr. Clayton is a Fellow of the New York Academy of Medicine. She currently serves on the FDA Advisory Panel for Ophthalmic Devices; the medical and scientific advisory board of Tissue Banks International; and the editorial board of *The Ocular Surface*. She was selected as a Silver Fellow by the Association for Research in Vision and Ophthalmology and a recipient of the Senior Achievement Award from the American Academy of Ophthalmology. Dr. Clayton has received several awards from her NIH peers in recognition of her leadership. She co-chairs the NIH Working Group on Women in Biomedical Careers with the NIH Director.

### **C. Neill Epperson, M.D.**

C. Neill Epperson, M.D., is an associate professor of psychiatry and obstetrics and gynecology and the Director of the Penn Center for Women's Behavioral Wellness at the Perelman School of Medicine of the University of Pennsylvania. Dr. Epperson received her undergraduate and medical degrees at the University of North Carolina at Chapel Hill. She completed her psychiatry residency training and postdoctoral research fellowship at Yale University, where she remained on faculty for 12 years before being recruited to Penn. Dr. Epperson's research interests are in the neuroendocrine basis for mood, behavior, and cognitive changes across the female lifespan. As the co-director for the Penn Center for the Study of Sex and Gender in Behavioral Health,

Dr. Epperson also investigates the contribution of sex to the pathogenesis and treatment of psychiatric and substance use disorders and cognitive aging.

### **Arpana Gupta, M.D.**

Arpana Gupta, Ph.D., received her Ph.D. in clinical neuropsychology from the University of Tennessee, Knoxville, and completed her clinical internship at Massachusetts General Hospital/Harvard Medical Center in 2010. Afterward, she went to the University of California, Los Angeles (UCLA) for her postdoctoral research training, and in 2012 she joined the neuroimaging and psychophysiological cores at UCLA's Oppenheimer Family Center for Neurobiology of Stress. Her research examines the influence of the brain, genetics, and psychosocial factors on the underlying pathophysiology of disorders with altered interoceptive processing (functional pain disorders and obesity). To help make an important step toward providing powerful and sensitive biomarkers for pain disorders, Dr. Gupta is dedicated to developing and testing biopsychosocial models that comprehensively address the interactions between psychosocial (e.g., early adverse life events, adult trauma, resilience, exercise, diet), environmental (socioeconomic status), and biological (genes, sex, race) factors in causing epigenetic changes and in shaping brain structure and function. She hopes that such biological readouts will bring to the forefront those groups and individuals who are at increased risk as a result of disadvantaged backgrounds and consequently altered neurobiologies.

### **Scott Hultgren, Ph.D.**

Scott Hultgren, Ph.D., is the Helen Lehbrink Stoevers Professor of Molecular Microbiology at Washington University in St. Louis, where he also serves as the inaugural Director of the Center for Women's Infectious Disease Research. He was elected to the National Academy of Sciences in 2011. He received his undergraduate education at Indiana University, his Ph.D. at Northwestern University in Chicago, and his postdoctoral training at Umeå University in Sweden, under the tutelage of Staffan Normark. He is also a Fellow of the American Association for the Advancement of Science (AAAS) and has been honored with a Distinguished Investigator Award at Washington University. In 1998, he received the Eli Lilly award, the preeminent microbiology award granted for investigators younger than 40. In 2012, he received the Fellows Award, which recognizes a distinguished individual for outstanding achievement in science, from the St. Louis Science Academy. He was the co-chair of "Moving into the Future: New Dimensions and Strategies for Women's Health

Research,” a national conference sponsored by ORWH/NIH and Washington University. His other honors include a Nobel Fellowship, an NIH Merit grant, an honorary Doctorate of Philosophy from Umeå University in Sweden, a Shipley Lectureship at Harvard University, and Chairmanship of a Gordon Conference on Microbial Attachment. Further, in honor of his dedication to teaching, he has been recognized as Washington University in St. Louis Course Master of the Year and Academic Women’s Network Mentor of the Year. Dr. Hultgren has mentored more than 50 individuals as pre- or post-doctoral trainees, fostering their success in establishing their own professional careers.

### **Carolyn M. Mazure, Ph.D.**

Carolyn M. Mazure, Ph.D., is a professor of psychiatry and psychology and Associate Dean for Faculty Affairs at Yale School of Medicine. Her research focuses on gender effects in onset, recurrence, and treatment response of stress-related disorders, especially depression, and addictive behaviors (smoking in particular). She is the Principal Investigator for Yale’s ORWH/NIDA/NIAAA-funded BIRCWH Scholar Program on Women’s Health and Addictive Behaviors; the Scientific Director of Yale’s ORWH/NIDA-funded SCOR to develop gender-sensitive treatments for tobacco dependence; and an Investigator on a Department of Veterans Affairs (VA)-funded grant studying gender differences in postdeployment addictive behaviors among returning combat veterans. She created and directs Women’s Health Research at Yale, the school’s interdisciplinary research center on health and gender. Since its creation in 1998, Women’s Health Research at Yale has become a leading center for initiating and supporting new studies to answer pressing questions on women’s health and gender differences, providing health data of practical benefit to the community, building research collaborations, and launching investigators into careers studying gender-specific aspects of health. Dr. Mazure has provided testimony to the U.S. Congress multiple times, and she served as a fellow for the Government Reform Committee. She also served on the planning committee for the First White House Conference on Mental Health and chaired the American Psychological Association’s Summit on Women and Depression.

### **Erin A. McClure, Ph.D.**

Erin A. McClure, Ph.D., is a behavioral psychologist with a background in preclinical and clinical investigation of substance use disorders and their treatment. Dr. McClure earned her B.S. in psychology

and neuroscience from Allegheny College in 2003 and her Ph.D. in psychology from the University of Florida in 2009. She is currently a postdoctoral fellow in the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina in Charleston. Dr. McClure is co-investigator on several National Institutes of Health-sponsored studies. Her research interests involve the study of relapse, withdrawal, craving, and treatment for nicotine and cannabis dependence through the use of outpatient, laboratory-based studies, as well as clinical trials assessing pharmacological and behavioral interventions. Dr. McClure is also interested in the utilization of different technology outlets to perform fine-grained analyses of the process of relapse to inform treatment efforts and deliver interventions in real time.

### **Sherry A. McKee, Ph.D. Clin.**

Sherry McKee, Ph.D. Clin., is an associate professor of psychiatry, Director of the Yale Behavioral Pharmacology Laboratory, and Clinical Director of the Forensic Drug Diversion (ForDD) Clinic, an outpatient treatment facility for addiction. She completed her graduate training at the University of Western Ontario, and she did research fellowships at the Addiction Research Foundation in Toronto, Canada, and at Yale University School of Medicine. Her research focuses on improving treatment for people with nicotine and alcohol use disorders. Using a transdisciplinary perspective, she utilizes various methodologies, including human laboratory paradigms, survey research, and epidemiological research, to uncover the mechanisms underlying poor outcomes and translate the findings into improved interventions. She is the Principal Investigator of a Specialized Center for Research (SCOR-P50), “Developing gender-sensitive treatments for tobacco dependence,” funded by the National Institute on Drug Abuse (NIDA) and the NIH Office of Research on Women’s Health. Her research achievements have been recognized by the Natural Sciences and Engineering Research Council of Canada, the Research Society for Alcoholism, NIDA, the Society for Research on Nicotine and Tobacco, the National Alliance for Research on Schizophrenia and Depression, and the American Psychological Association.

### **Melissa Morrow, Ph.D.**

Melissa (Missy) M. Morrow, Ph.D., is an NIH K12 BIRCWH Scholar, an assistant professor of biomedical engineering, and a research associate in orthopedic surgery at Mayo Clinic. She received her doctoral degree in biomedical engineering from Mayo



Clinic College of Medicine and her B.S.E. from Tulane University. Dr. Morrow's research is focused on investigating causes, treatments, and outcomes of musculoskeletal diseases and disorders, with a special emphasis on women's musculoskeletal health. Using advanced techniques in laboratory motion analysis, field-based activity monitoring, and imaging, she is examining knee osteoarthritis, joint replacement, and shoulder impingement. During her tenure as a BIRCWH Scholar, Dr. Morrow is investigating sex differences in knee osteoarthritis. Osteoarthritis of the knee is a leading cause of disability in the United States, and while both men and women are diagnosed with knee osteoarthritis at troubling rates, its prevalence and incidence are higher among women than among men. The goal of Dr. Morrow's research is to characterize the differences in disease severity, manifestation, and outcomes between men and women with knee osteoarthritis.

### **Jason Moser, Ph.D.**

Jason Moser, Ph.D., is currently an assistant professor in the Department of Psychology at Michigan State University, where he directs the Clinical Psychophysiology Lab. He received his degree in psychology (clinical) from the University of Delaware in 2009, after completing a one-year clinical internship at the Boston Consortium in Clinical Psychology. Dr. Moser's research focuses on how anxiety affects cognitive functioning. Using methods from cognitive neuroscience and neuroendocrinology, Dr. Moser investigates how basic functions such as error processing and attention are disrupted in anxious individuals and the extent to which sex hormones contribute to this dysfunction. Current avenues of study include both how ovarian hormones contribute to the relationship between anxiety and error-related brain activity and sex differences in the relationship between anxiety and error-related brain activity. More broadly, Dr. Moser studies how the different ways people think affect cognitive and emotional processes. His work examines how negative ways of thinking—worry—and positive ways of thinking—looking on the bright side and believing in the ability of the self and others to change and grow—affect reactions to mistakes and attention, as well as a person's ability to manage emotions.

### **Joan Davis Nagel, M.D, M.P.H.**

Joan Davis Nagel, M.D., M.P.H., is a Medical Officer in the Office of Research on Women's Health and serves as Director of Interdisciplinary Research Programs. She is Program Director of the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Mentored Scientist Career

Development Program and the ORWH Scientific Coordinator for the Specialized Centers of Research (SCOR) on Sex Differences. BIRCWH programs support junior faculty who have recently completed clinical training or postdoctoral fellowships and are conducting interdisciplinary basic, translational, and/or clinical or health services research relevant to women's health. The 11 SCOR Centers are conducting research on the role of sex/gender in conditions such as depression, pain, addiction, metabolic disorders, musculoskeletal conditions, urinary tract, reproductive health, and aging. Dr. Nagel earned a B.A. in biology from Williams College, an M.D. from the State University of New York at Buffalo's School of Biomedical Sciences, and an M.P.H. from the Johns Hopkins School of Hygiene and Public Health. Her background includes training in obstetrics/gynecology, as well as a preventive medicine residency that she completed at the Johns Hopkins Medical Institutions in Baltimore, MD. Before assuming her current role, she was Medical Officer for three years in the Reproductive Sciences Branch at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), overseeing a portfolio of women's health research and career development grants. She also served for two years as one of the first Project Team Leaders for the NIH Roadmap's Multidisciplinary Clinical Research Career Development Program to re-engineer the clinical research enterprise and was Director of the NICHD's Contraception and Infertility Research Loan Repayment Program. Prior to coming to the National Institutes of Health, Dr. Nagel worked as a physician for the New York City Department of Health's Bureau of Sexually Transmitted Diseases and as a medical consultant for the Urban Women's Retreat, a shelter for survivors of domestic violence in Harlem, NY.

### **Kathleen M. O'Leary, M.S.W.**

Kathleen M. O'Leary, M.S.W., is Chief of the Women's Program at the National Institute of Mental Health. After receiving her B.A. in social work, she worked with infants in foster care and children in residential treatment before obtaining her M.S.W. from Smith College School for Social Work. She has worked for NIMH for over 30 years, as a research clinician studying adolescent mothers, study coordinator for the intramural borderline personality disorder study, supervisor of clinicians working with patients with schizophrenia, and supervisor of clinicians on the NIMH patient recruitment and protection team. Her publications include studies on adolescent pregnancy, depression, and neuropsychological deficits in borderline personality disorder, as well as two book chapters on personality disorders. Serving in the Office of Research on

Disparities and Global Mental Health since 2005, she works closely with NIH and HHS offices on research initiatives on perinatal mental health, sex differences research, health disparities, the mental health of military women, and the mental health effects of violence against women.

### **Estella Parrott, M.D., M.P.H.**

Estella Parrott, M.D., M.P.H., joined the staff of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development in 1998. She was recently appointed to the newly established Gynecologic Health and Disease Branch as a Medical Officer. Examples of research topic areas covered by this portfolio include disorders of the menstrual cycle, chronic pelvic pain, and vulvodynia. Research initiatives that are important to quality-of-life issues across women's reproductive lifespan encompass pelvic floor disorders, endometriosis, and uterine fibroids. Special areas of emphasis include reproductive concerns at the perimenopause and menopause transition, adolescent gynecology, and disparities in the incidence of gynecologic disorders across underserved populations. An important focus of the portfolio is the promotion of the independent careers of physician-scientists who can address research opportunities relevant to women's reproductive health. A native of New York City, Dr. Parrott received an undergraduate degree in biology from the City College of New York. Before embarking on a medical career, she earned a master's degree from the University of Chicago. Dr. Parrott received her degree in medicine from the University of Illinois College of Medicine, and she did a residency in obstetrics and gynecology at Cook County Hospital in Chicago. She is board certified in obstetrics and gynecology and is a Fellow of the American College of Obstetricians and Gynecologists. She also secured a master's degree in public health from the George Washington University. Dr. Parrott has held other federal government positions with the National Institute of Allergy and Infectious Diseases, the Food and Drug Administration, and the Health Resources and Services Administration.

### **Julienne Rutherford, Ph.D.**

Julienne Rutherford, Ph.D., is a biological anthropologist at the University of Illinois at Chicago (UIC). She teaches maternal physiology to nurse midwifery and women's health nurse practitioner master's students in the Department of Women, Children, and Family Health Science at the UIC College of Nursing. She also is an assistant professor

in the Graduate College and an adjunct assistant professor in the UIC Department of Anthropology.

### **Aditi Saxena, M.D.**

Aditi Saxena, M.D., is a board-certified endocrinologist, a faculty member at Brigham and Women's Hospital (BWH) and Harvard Medical School (HMS), and a member of the Institutional Review Board at BWH. She received formal training in conducting patient-oriented research through the Scholars in Clinical Sciences Program at HMS and graduated with an M.S. Dr. Saxena has served as principal investigator and co-investigator on several clinical studies examining hormonal phenotypes in relation to vascular dysfunction in both women and men. Dr. Saxena and colleagues demonstrated that although women with history of preeclampsia return to a normotensive state postpartum, they demonstrate salt sensitivity of blood pressure and increased sensitivity to angiotensin II postpartum. As a BIRCWH Scholar since 2011, Dr. Saxena has continued to study postpartum women with prior preeclampsia to further examine abnormalities in the renin-angiotensin system in these women. By studying exposures and their hormonal influences during pregnancy in relation to their postpartum effects, Dr. Saxena hopes to both identify the novel mediators of cardiometabolic disease in women and set the stage for implementing strategies to decrease future risk in these patients. During her involvement in the Harvard BIRCWH Scholars Program, Dr. Saxena has broadened her research focus through collaborations with other investigators, examining the relationship of endocrine-disrupting chemicals with cardiovascular risk factors in men and women.

### **Pamela Scott, Ph.D.**

Pamela E. Scott, Ph.D., is the Director of Research and Development at the U.S. Food and Drug Administration (FDA) Office of Women's Health (OWH). An epidemiologist and statistician, Dr. Scott has over 20 years of experience developing and leading research to address women's health issues, such as the inclusion of women in clinical trials, the impact of sex and gender differences on the safety and efficacy of FDA-regulated products, and the risks of drug exposure during pregnancy. Dr. Scott currently leads the OWH's regulatory research program and is responsible for advocating and promoting the participation of women in clinical trials and for sex, gender, and subpopulation analyses. Dr. Scott led the FDA's evaluation and drafting of the congressionally required report for Section 907 of the Food and Drug Administration Safety and Innovation Act on the inclusion and analysis of women and other



demographic subgroups in clinical studies supporting the approval of FDA-regulated medical products. The report was released by FDA in August 2013. Prior to joining OWH, Dr. Scott developed and managed several research programs at the FDA, including the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), a FDA-funded research program designed to conduct epidemiological studies of the risk of medication exposure during pregnancy and the resulting birth outcomes.

Dr. Scott received her Ph.D. in epidemiology (with a concentration in clinical trials methodology) from the Bloomberg School of Public Health at Johns Hopkins University. She also holds a M.A. in statistics from American University.

### **Tomoko Udo, Ph.D., M.Sc.**

Tomoko Udo, Ph.D., received her M.S. in neuroscience and her Ph.D. in public health from Rutgers University. She completed her postdoctoral training at the Center of Alcohol Studies at Rutgers University and is currently an associate research scientist at Yale University School of Medicine. In 2011, she joined Yale's BIRCWH program to build a research program to understand the overlaps between drug abuse and obesity, in hopes of identifying new sex-sensitive therapeutic targets for both disorders. She is particularly interested in identifying the factors that may disrupt or enhance self-control. Her research utilizes both animal and human laboratory models to explore the neurobiological systems involved in self-control and decision making in appetitive behaviors. Using a rodent model of binge eating, she is currently investigating the biological systems responsible for sex differences in regulation of food intake in general, in addition to those involved in binge-eating behaviors. Through a human laboratory model, she is looking at whether sex differences exist in the relationship between self-control, appetite-regulating hormones, and eating behaviors.

### **Digna R. Velez Edwards, Ph.D.**

Digna R. Velez Edwards, Ph.D., is a genetic epidemiologist and an assistant professor in the Department of Obstetrics and Gynecology at Vanderbilt University. Dr. Velez Edwards received her masters in applied statistics (2007) and her Ph.D. in human genetics (2008) from Vanderbilt University, with subsequent postdoctoral training in human genetics at the University of Miami (2008-2009). She has established a research program focused on genetic and environmental risk factors associated with women's health and reproductive outcomes. Since the start of her faculty appointment, Dr. Velez Edwards

has developed and coordinated a repository of biospecimens from participants in the Right from the Start pregnancy cohort for use in genetic epidemiology studies examining reproductive health complications and risk for adverse pregnancy outcomes. She has several ongoing research projects utilizing this resource, as well as large clinical databases that link clinical information to DNA. These studies focus on understanding the racial and/or ethnic disparities in genetic risk for several complex conditions, including preterm birth, miscarriage, uterine fibroids, and pelvic organ prolapse.

### **Lisa Privette Vinnedge, Ph.D.**

Lisa Privette Vinnedge, Ph.D., is a Research Instructor in the Department of Oncology in the Cancer and Blood Diseases Institute at Cincinnati Children's Hospital Medical Center. She is also a BIRCWH (K12) scholar with the University of Cincinnati Center for Clinical and Translational Science and Training. She received her Ph.D. in human genetics, with a focus on cancer genetics, from the University of Michigan Rackham Graduate School in 2008.

Her research uses both murine and human models to identify and characterize the molecular mechanisms that drive breast cancer progression and chemotherapeutic drug resistance. Her current focus is on the role of the DEK oncogene and how it directs tumor growth and metastasis through the Wnt signaling pathway. She also has a particular interest in studying the breast cancer stem cell population, which is responsible for disease progression and recurrence. In addition to the BIRCWH award, she has recently received funding from the Marlene Harris Ride Cincinnati Foundation to continue her studies on drug resistance in breast cancer stem cells.

Her career development goals include advancing her knowledge in flow cytometric techniques to study cancer stem cells, uses of murine models of breast cancer, and high-throughput biochemical assays. Dr. Vinnedge's long-term career goal is to identify and test novel therapeutic drug targets in order to prevent disease progression and recurrence.

### **Cora Lee Wetherington, Ph.D.**

Cora Lee Wetherington, Ph.D., joined NIDA in 1987. Since 1995, she has been NIDA's Women and Sex/Gender Differences Research Coordinator, chairing NIDA's Women and Sex/Gender Differences Research Group and serving as NIDA's representative to the NIH Coordinating Committee of the Office of Research on Women's Health. Her activities are aimed at advancing and incorporating the study of



women and sex/gender differences into all areas of drug abuse research. Dr. Wetherington also serves as a program officer in NIDA's Behavioral Sciences Research Branch within the Division of Basic Neuroscience and Behavioral Research, where she oversees a program of extramural preclinical research that includes the study of sex differences, vulnerability to drug abuse, and the behavioral and neurobiological effects of exposure to drugs throughout the lifespan.

For her efforts in promoting research on women and sex/gender differences in drug abuse, Dr. Wetherington received the Meritorious Research Service Commendation from the American Psychological Association Board of Scientific Affairs in 2005 and the J. Michael Morrison Award from the College on Problems of Drug Dependence in 2010. She serves on the board of editors of *Clinical and Experimental Psychopharmacology* and on the editorial board of *NIDA Notes*, a position she has held since 1988. She is coeditor of three books, including *Drug Addiction Research and the Health of Women*.

Dr. Wetherington received her Ph.D. in experimental psychology from the University of North Carolina at Greensboro in 1976. Prior to joining NIDA, she was a psychology professor at the University of North Carolina at Charlotte, where for 12 years, funded in part by NIH and National Science Foundation grants, she conducted research in the field of animal learning and behavior.





## SELECT BIRCWH AND SCOR POSTERS

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### BIRCWH Posters

**P-1: Predictors of Neonatal Neurologic Birth Depression and Intraventricular Hemorrhage in Preterm Premature Rupture of Membranes**

Jennifer Armstrong-Wells, University of Colorado, Denver

**P-2: Maternal Smoking and the Impact on Infant Weight at 9 Months**

Susan Braid, University of Maryland

**P-3: Evaluate Perineal Body Property in vivo Using Ultrasound Elastography Technique: Method Development and Preliminary Finding in Nulliparous Women**

Luyun Chen, University of Michigan

**P-4: Subjective and Physiological Responses to IV Nicotine: Effects of Sex and Menstrual Phase**

Elise E. DeVito, Yale University

**P-5: Change in Sexual Orientation Identity During Young Adulthood Predicts Higher Depressive Symptoms: Results from a Nationally Representative Longitudinal Study**

Bethany Everett, University of Illinois at Chicago

**P-6: Altered Th1/Th2 Cytokines in Pregnancy and Risk for Postpartum Anxious Depression**

Constance Guille, Medical University of South Carolina

**P-7: Regional Variation in HPV Vaccination Among 9–17 Year Olds**

Jacqueline Hirth, University of Texas

**P-8: Born Too Soon: Trends in Childbirth Before 39 Weeks Gestation Without Medical Indication, 1995–2009**

Katy B. Kozhimannil, University of Minnesota

**P-9: Air Pollution Exposures and Incident Infertility in the Nurses Health Study II**

Shruthi Mahalingaiah, Boston University

**P-10: Sex Differences in Estrogen Receptor/LOX-1 Signaling in Mouse Aortic Smooth Muscle Cells**

Milton H. Hamblin, Tulane University

**P-11: Estradiol Increases IL-17A Protein Expression from Mouse CD4+ Th17 Differentiated Cells**

Dawn C. Newcomb, Vanderbilt University

**P-12: Maternal Intake of Supplemental Iron and Risk for Autism Spectrum Disorders**

Rebecca J. Schmidt, University of California, Davis

**P-13: A Next Generation Sequencing (NGS) Method to Identify HPV16 Integration Sites in Human Cervical Cancer**

Julie Schwarz, Washington University, St. Louis

**P-14: Risk Factor Differences for Female Adolescent Iron Deficiency as Defined by Body Iron and Ferritin Models**

Deepa Sekhar, Pennsylvania State University

**P-15: Managing the Competing Demands of Low-wage Employment and Breast Cancer Treatment**

Robin C. Vanderpool, University of Kentucky



## SCOR Posters

**P-16: Ovarian Hormone Suppression in Premenopausal Women Reduces Fat-free Mass and Resting and 24-h Energy Expenditure**

Kathleen Gavin, University of Colorado, Denver

**P-17: Guanfacine Has Antidepressant-like Effects and Potentiates Nicotinic-based Antidepressants**

Yann S. Mineur, Yale University

**P-18: Gender Differences in Subjective Responses to Yohimbine Administration Between Cocaine-dependent Men and Women**

Megan M. Moran-Santa Maria, Medical University of South Carolina

**P-19: Animal Studies of Sex Differences and Hormonal Influences on Positive and Negative Effects of Drug Abuse and Its Treatment**

Marilyn E. Carroll, University of Minnesota

**P-20: Neurobiology of Resilience – Personality and Functional Connectivity of the Default Mode and Salience Networks**

Joshua Istrin, University of California, Los Angeles

**P-21: Sex, Strain, and Regional Differences in the Colonic Epithelial Response to Repeated Water Avoidance Stress (rWAS)**

Muriel Larauche, University of California, Los Angeles

**P-22: Bladder Exfoliation Response to E. coli Infection Exposes New Receptors Bound by FmID: Multi-phasic Colonization Maintains Chronic UTI**

Matt S. Conover, Washington University, St. Louis

**P-23: Positive Selection Analysis Identifies a Role for Arginine Metabolism in Chronic Bladder Colonization by Uropathogenic E. coli**

Michael E. Hibbing, Washington University, St. Louis

**P-24: A New Murine Model of Urinary Tract Infection Identifies Sex Differences in Pathogenesis**

Patrick D. Olson, Washington University, St. Louis

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# SPECIALIZED CENTERS OF RESEARCH (SCOR) ON SEX DIFFERENCES\* FY 2012–2016

## INSTITUTION & INVESTIGATOR

## SCOR THEME

Mayo Clinic Virginia Miller, Ph.D.	Sex-Specific Risk for Vascular Dysfunction and Cognitive Decline
**Medical University of South Carolina Kathleen Brady, M.D., Ph.D.	Sex and Gender Differences in Addictions and Stress Response
**Northwestern University Andrea Dunaif, M.D.	Genes, Androgens and Intrauterine Environment in PCOS
University of California, Davis Nancy Lane, M.D.	Sex Differences in Musculoskeletal Conditions across the lifespan
**University of California, Los Angeles Emeran Mayer, M.D.	Center for Neurovisceral Sciences and Women's Health (Sex Differences in Pain)
University of Colorado Wendy Kohrt, Ph.D.	Metabolic Consequences of Loss of Gonadal Function
**University of Michigan, Ann Arbor John DeLancey, M.D.	Birth, Muscle Injury and Pelvic Floor Dysfunction
University of Minnesota Marilyn Carroll, Ph.D.	Sex Differences and Progesterone effects on Impulsivity, Smoking and Cocaine Stress
University of Pennsylvania C. Neill Epperson, M.D.	Pre-pubertal Stress, Windows of Risk and Sex Bias for Affective Disturbance
**Washington University Scott Hultgren, Ph.D.	Molecular and Epidemiologic Basis of UTI in Women
Yale University Sherry McKee, Ph.D.	Gender-Sensitive Treatment for Tobacco Dependence

\*title change for centers

\*\*competitive renewal



# SPECIALIZED CENTERS OF RESEARCH ON SEX AND GENDER FACTORS AFFECTING WOMEN'S HEALTH FY 2007–2011

## INSTITUTION & INVESTIGATOR

## SCOR THEME

Brigham and Women's Hospital  
Jill Goldstein, Ph.D.

Fetal antecedents to sex differences in depression:  
a translational approach

Medical University of South Carolina  
Kathleen Brady, M.D., Ph.D.

Role of sex and gender differences in substance  
abuse relapse

Northwestern University  
Andrea Dunaif, M.D.

Excess male hormones (androgens) as the key to  
explaining polycystic ovarian syndrome (PCOS)

University of California, Los Angeles  
Emeran Mayer, Ph.D.

A coordinated study of stress, pain, emotion, and sexual  
factors underlying the pelvic visceral disorders of irritable  
bowel disorder and interstitial cystitis

University of California, San Francisco  
Jeanette Brown, M.D.

Lower urinary tract function in women

University of Chicago  
David Ehrmann, M.D.

Sex steroids, sleep, and metabolic dysfunction in women

University of Miami  
Emmalee Bandstra, M.D.

Sex and gender influences on addiction and health:  
a developmental perspective

University of Michigan, Ann Arbor  
John DeLancey, M.D.

Birth, muscle injury and pelvic floor dysfunction

University of Missouri, Kansas City  
Hong-Wen Deng, Ph.D.

Identifying the genes that put women at risk  
for osteoporosis

Washington University  
Scott Hultgren, Ph.D.

Molecular and epidemiologic basis of acute and  
recurrent urinary tract infections (UTI's) in women

Yale University  
Rajita Sinha, Ph.D.

Sex, stress, and substance use disorders

# SPECIALIZED CENTERS OF RESEARCH ON SEX AND GENDER FACTORS AFFECTING WOMEN'S HEALTH FY 2002–2007

## INSTITUTION & INVESTIGATOR

## SCOR THEME

Emory University  
Zachary Stowe, M.D.

Pharmacology of Anti-epileptic and Psychotropic Medications during Pregnancy and Lactation

Northwestern University  
Andrea Dunaif, M.D.

Genes, Androgens, and Intrauterine Environment in Polycystic Ovarian Syndrome

University of Michigan, Ann Arbor  
John DeLancey, M.D.

Birth, Muscle Injury, and Pelvic Floor Dysfunction

University of Pittsburgh  
Gerald Schatten, Ph.D.

Genetic and Environmental Origins of Adverse Pregnancy Outcomes

University of Washington  
Jashvant Unadkat, Ph.D.

Mechanisms by Which Drug Transporters Alter Maternal and Fetal Drug Exposure during Pregnancy

University of California, Los Angeles  
Emeran Mayer, M.D.

Sex and Gender Factors in the Pathophysiology of Irritable Bowel Syndrome and Interstitial Cystitis

University of Maryland  
Joel Greenspan, Ph.D.

Sex Differences in Pain Sensitivity

University of California, San Francisco  
Janette Brown, M.D.

Mechanisms Underlying Female Urinary Incontinence

Washington University  
Scott Hultgren, Ph.D.

Molecular and Epidemiologic Basis of Acute and Recurrent Urinary Tract Infections in Women

Medical University of South Carolina  
Kathleen Brady, M.D., Ph.D.

Role of Sex and Gender Differences in Substance Abuse Relapse

Yale University  
Rajita Sinha, Ph.D.

Sex, Stress, and Cocaine Addiction



## BIRCWH Program Sites, 2000–2013



Nagel, JD, Koch, A, Guimond, JM, Glavin, S, Geller, S. "Building the Women's Health Research Workforce: Fostering Interdisciplinary Research Approaches in Women's Health". Global Advances Health and Medicine, Vol. 2, Number 5, September 2013















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